

Ibandronate associated Fixed Drug Eruption

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ABSTRACT:

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Ibandronate is a monthly oral bisphosphonate, which is a goal standard treatment of osteoporosis. It's common adverse events included back pain, upper respiratory tract infection, and dyspepsia. It has never been reported as fixed drug eruption before. We have found a patient who developed fixed drug eruption after taking Ibandronate in dermatologic clinic of Bamrasnaradura Infectious Diseases Institute

Key word: Ibandronate, fixed drug eruption

บทคัดย่อ:

แพรวพรรณ นุณยรัตพันธุ์, พรชัย จิระชนากุล อาการทางผิวหนังแบบFIXED DRUG ERUPTIONที่เกิดหลังจากได้ยา IBANDRONATE. วารสารโรคผิวหนัง 2554; 27: 130-134.

กลุ่มงานบริการเฉพาะทาง งานผู้ป่วยนอก สถาบันบำราศนราดูร

Ibandronate เป็นยาในกลุ่มBisphosphonate ที่ใช้รักษาโรคกระดูกพรุน โดยรับประทานเดือนละครั้ง ผลข้างเคียงที่พบบ่อย คือ อาการติดเชื้อทางระบบหายใจส่วนต้น อาการปวดหลัง และปวดท้องเป็นต้น ผู้เขียนได้รายงานผู้ป่วยที่เกิดอาการทางผิวหนังแบบ fixed drug eruption หลังได้รับยา Ibandronate ซึ่งไม่เคยมีรายงานมาก่อน

คำสำคัญ : Ibandronate, fixed drug eruption

Introduction

Osteoporosis characterized by low bone mass and structural deterioration of bone tissue, which caused decreasing bone strength and in-turn possibility of fractures. Bisphosphonates, such as Alendronate, Risedronate, Ibandronate and Zoledronate, is a gold standard treatment of osteoporosis. It is an agent that inhibit bone resorption and required long-term use for optimal and sustained therapeutic benefit. In order to increase compliance of bisphosphonate therapies, the longer dose-free intervals, such as oral once monthly, were developed. Ibandronate (Boniva) is once a month oral bisphosphonate, which has been approved by FDA 150 milligram once a month of Ibandronate is used to prevent and treat osteoporosis in women after the menopause. Common side effects of Ibandronate that have been reported include back pain (13.5%), arthralgia (3.2%), bronchitis (10%), dizziness (3.7%), fever (9%), headache (6.5%), myalgia (5.7%), upper

respiratory infection (33.7%), dyspepsia (12%) and diarrhea (10%). Moreover, it may cause allergic reactions (2.5%) which included a sudden severe drop in blood pressure, rapid heart rate, skin rash, itching and hives but there has not been reported of fixed drug eruption.^{1,2,3}

Fixed Drug Eruption (FDE) is a skin inflammation which is induced by skin-resident intraepidermal CD8 T cells. It is characterized by a single solitary or a small number of pruritic well circumscribed erythematous macules or plaque. These lesions typically develop at exactly the same sites with each administration of the causative drug, food or chemical substances. However, after the drug has been discontinued, the lesions are spontaneously resolved with residual hyperpigmentation. The lesions usually flare within 30 min to 8 h after drug administration. Burning sensation often occur with the lesion. Fixed drug eruption can appear anywhere on the skin or mucous membrane, the most commonly affected sites are lips, palms, soles,

extremities and groin areas. The drugs that commonly reported to cause fixed drug eruption are: cotrimoxazole, tetracycline, metamizole, phenylbutazone, paracetamol, acetylsalicylic acid, NSAIDs, metronidazole, tinidazole, chlormezanone, amoxicillin, ampicillin, erythromycin, belladonna, griseofulvin, phenobarbitone, diflunisal, pyrantel pamoate, clindamycin, allopurinol, orphenadrine, albendazole, dapsone, phenolphthalein, oral contraceptives, phenacetin, doxycycline, minocycline, panmycin, sulfonamide, sulfasalazine, benzodiazepines and chlordiazepoxide, hyoscine butylbromide, and quinine.^{4,5,6} A skin biopsy has shown hydropic degeneration of the epidermal basal cells and pigmentary incontinence.⁷

We have found an unusual case of patients who developed fix drug eruption after taking Ibandronate.

Case Report

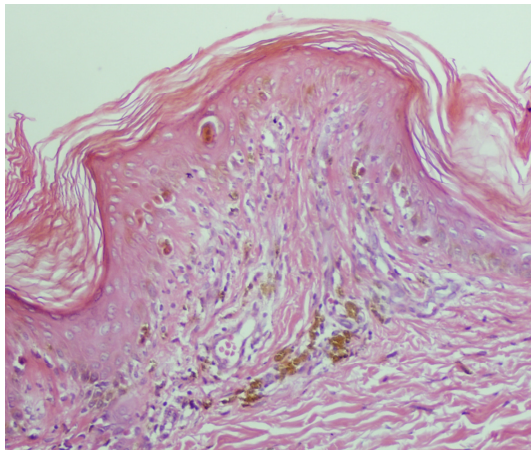
A 72-year old Thai female came to skin clinic of Bamrasnaradura Infectious Disease Institute on December 21st, 2010 with multiple discrete hyperpigmented patches on her left thigh, waist and lips areas.

She was healthy and diagnosed as osteoporosis 2 years ago, at Bamrasnaradura Infectious Diseases Institute, and started treatment with calcium carbonate, glucosamine, Alendronate since then. Her attending physician suggested substitute Alendronate on May 2010 with Ibandronate on June 20th, 2010. Then she took Ibandronate once a month.

On September 23rd, 2010, 3 days after taking Ibandronate, she observed multiple erythematous patches on her left thigh and her lower lip. She felt itchy but didn't take any medication nor apply any medication on her skin lesions. A week later, her symptoms were resolved. The lesions became darker to brownish patches. On October 20th, 2010, she took Ibandronate again. As a result, 3 days after that, her old hyperpigmented patches became erythema and itchy again on October 23rd, 2010. And there was a few patches developing on right side of her waist. It was also red and itching. She took Cetirizine and applied Bethametasone cream on her lesions this time, and all symptoms were gone after a few days but left her hyperpigmented patches finally. In November, she stopped taking Ibandronate. She said there is neither any symptom nor new lesions, but all previous hyperpigmented patches still remained. Then, she started taking Ibandronate again on December 13rd, 2010. Then again 3 days afterwards, all her hyperpigmented patches on her lower lip waist and thigh became itchy and red again. She suspected that her symptoms were caused by Ibandronate, she visited a dermatologist at Bamrasnaradura Infectious Diseases Institute on December 21st, 2010.

On examination, December 21st, 2010, the patient had three brownish patches on her lip area, right side of waist and left inner thigh without any symptoms. Her current medications are Ibandronate, Caltrate and Viatril-S, no other vitamin or supplement. Fixed drug

eruption was diagnosed and topical steroid was prescribed. Skin biopsy was not done due to patient decision.



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Figure1: Fixed drug eruption(10X). Dyskeratotic keratinocytes are present in the basal layer and also hydropic degeneration.



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Figure 2A: Fixed drug eruption associated with Ibandronate at lip area



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Figure 2B: Fixed drug eruption associate with Ibandronate at right side of waist area



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Figure 2C: Fixed drug eruption associate with Ibandronate at left inner thigh area

Discussion

We reported the first case of fixed drug eruption due to Ibandronate. Both Alendronate [C₄H₁₂NNaO₇P₂·3(H₂O)] and Ibandronate (C₉H₂₂O₇NP₂Na) are nitrogen-containing bisphosphonates. Fixed drug eruption, therefore, may be caused by the difference in chemical structure or other component and substance in Ibandronate formulation. Most of the patient reported fixed drug eruption after 3-8 hours of exposure lesion appeared after taking Ibandronate for 3 days (72 hours) and her first symptom appeared after she used Ibandronate for 3 months (three episodes). It may occur due to the fact that fixed drug eruption initially appears when susceptible patient is sensitized to particular drug, and the lag period is highly variable depending on patients, ranging from a few weeks to several years.⁴

Nevertheless, Ibandronate becomes more widely administration due to better adherence and compliance to treatment. Physician should aware of fixed drug eruption as a possible reaction of Ibandronate.

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